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09/161,680    09/28/98    BORNSCHEUER

U    48429

EXAMINER

HM12/1211

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ART UNIT

PAPER NUMBER

1652

DATE MAILED:

12/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.

09/161,680

Applicant(s)

Bornscheuer et al.

Examiner

Kathleen Kerr

Group Art Unit

1652



☒ Responsive to communication(s) filed on 10/16/00

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1, 2, 4-7, 10, and 11 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1, 2, 4-7, 10, and 11 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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## **DETAILED ACTION**

### ***Application Status***

1. In response to the non-final Office action (Paper No. 12), an amendment was filed on October 16, 2000. Said action rejected all claims, claims 1-2 and 4-9, which were considered. Applicants' newly filed amendment canceled claims 8 and 9, amended claims 1 and 4, and added new claims 10-11. Newly added claims 10-11 are drawn to the originally examined invention.

Claims 1-2, 4-7, and 10-11 are pending in the instant application and will be examined in this Office action

### ***Withdrawn - Objections to the Claims***

2. The previous objection to Claim 1 to for an informality is withdrawn by virtue of Applicants' amendment to the instant claim.

3. The previous objection to Claims 4, 8, and 9 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is withdrawn by virtue of Applicants' amendment and/or cancellation of the instant claims.

The Examiner notes that new Claim 10 is drawn to the same subject matter as canceled Claim 9; see NEW REJECTIONS below.

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***Withdrawn - Claim Rejections - 35 U.S.C. § 112***

4. Previous rejection of Claim 1, and dependent claims 2 and 4-9, under 35 U.S.C. 112, second paragraph, for the indefinite term "impeding activity" and for cumbersome language, is withdrawn by virtue of Applicants' amendment to the instant claims and by virtue of the Examiner's reconsideration in view of the specification as cited by Applicants (see Paper No. 13, page 3, first full paragraph).

5. The previous rejection of Claim 8, and dependent claim 9, under 35 U.S.C. 112, second paragraph, is withdrawn by virtue of Applicants' cancellation of said claims.

6. The previous rejection of Claim 1, and dependent claims 2 and 4-9, under 35 U.S.C. 112, first paragraph, enablement, is withdrawn by virtue of Applicants' cancellation of the instant claims and/or the Examiner's reconsideration. Applicants' arguments have been considered but are not deemed persuasive so the Examiner has also written a Response to Arguments below.

***Withdrawn - Claim Rejections - 35 U.S.C. § 102 and 103***

7. The rejection of claim 4 under 35 U.S.C. 102(b) as being anticipated by Greener et al. is withdrawn by virtue of Applicants' amendment to said claim.

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8. The previous rejection of Claim 8 under 35 U.S.C. 102(b) as being anticipated by Greener et al. is withdrawn by virtue of Applicants' cancellation of said claim.

9. The previous rejection of Claim 9 under 35 U.S.C. 103(a) as being unpatentable over Greener et al. in view of Wilks et al. is withdrawn by virtue of Applicants' cancellation of said claim. The Examiner notes that new Claim 10 is drawn to the same subject matter as canceled Claim 9; see NEW REJECTIONS below.

***Maintained - Claim Rejections - 35 U.S.C. § 102***

10. The rejection of claims 1-2 and 5-7 under 35 U.S.C. 102(b) as being anticipated by Greener et al. is maintained by the Examiner. See Response to Arguments below.

***Response to Arguments***

11. The previous rejection of Claim 1, and dependent claims 2 and 4-9, under 35 U.S.C. 112, first paragraph, enablement, is withdrawn. Applicants' have canceled claims 8-9; the Examiner has reconsidered the rejection of Claims 1-2 and 4-7. Applicants' arguments have been considered but are not deemed persuasive for the following reasons.

Applicants argue that their invention is independent of enzyme source and to limit the instant claims to a particular source would deprive Applicants of the full protection of the invention.

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The Examiner notes that the rejection was based on the fact that Applicants have enabled *neither* their particular example or *any* other example within the scope of the invention due to the randomness of the instant methods. The Examiner reprints a pertinent part of the previous rejection below (see Paper No. 12, section 11):

"The instant claims are broadly drawn to methods which create enzymes having altered substrate specificity using a strain of bacteria, *Escherichia coli* strain XL1 Red, which strain randomly introduces mutations into DNA and which is commercially available and commonly used by skilled artisans to produce random mutations. While applicants include a single, effective example of the instant methods, the ability to alter an enzyme's substrate specificity by *random* mutation, without any selective pressure on the mutagenesis, is wholly and entirely unpredictable as indicated by the word *RANDOM*. Applicants' methods, while requiring a selective medium, do not indicate how a particular compound (i.e., enzyme substrate) in the growth medium of the mutating bacteria directs the random mutagenesis to particularly and predictably alter the enzyme's substrate specificity. This lack of predictability is especially poignant when considering that the linear DNA sequence of the average encoded protein contains no structural relationship to the particular positions of the encoded residues involved in the substrate specificity of the enzyme. Thus, it would be impossible to predictably direct random mutagenesis on DNA to particularly alter an encoded enzyme's substrate specificity."

Applicants' traversal does not address the pertinent issue of the unpredictability of the claimed methods. However, while the Examiner maintains that such experimentation is random and unpredictable, when such experimentation is easily testable and when only productive (substrate specificity altering) experimentation reads on the instant claims, said experimentation is not considered undue. The method is possible, although uncertain, since both Applicants and the art have examples of the instant method. Thus, the Examiner withdraws the instant rejection.

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12. The previous rejection of claims 1-2 and 5-7 under 35 U.S.C. 102(b) as being anticipated by Greener et al. is maintained. Applicants' arguments have been considered but are not deemed persuasive for the following reasons.

Applicants argue that Greener et al. do not disclose a method of altering substrate specificity. As previously stated in response to this argument (see Paper No. 12, section 12), the Examiner disagrees.

"The alteration in specific activity [taught by Greener et al.] would inherently be recognized as an alteration in substrate specificity by one of skill in the art since the commonly held definition of substrate specificity in the art is directly correlated with enzymatic (specific) activity wherein substrate specificity =  $k_{cat}/K_m$  and  $k_{cat}$  = enzymatic (specific) activity. Thus, the inherent matter is necessarily present in the prior art reference and an ordinarily skilled artisan would recognize this fact."

Applicants argue that Greener et al. does not teach Applicants' step 1(c). The Examiner disagrees. As previously stated, Greener et al. teach "screening for phenotypic variants of said gene in a nonmutator host organism, specifically *E. coli*" (see Paper No. 7, section 6). Said screening procedure is *inherently* absent of an impeding enzyme activity, especially considering Applicants' broad definition of "impeding" as found on pages 6-7, bridging paragraph, or said screening would not be productive. Also, Applicants state in their traversal of the 103 rejection that "Greener et al. do disclose the c) step of the instant claimed process" (emphasis added) (see Paper No. 13, pages 4-5, bridging paragraph).

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13. Although the previous rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Greener et al. in view of Wilks et al. is withdrawn, said rejection is relevant to new or amended claims 4 and 10-11 (see below), and thus Applicants' traversal of the rejection against claim 9 will be responded to here. Applicants' arguments have been considered but are not deemed persuasive for the following reasons.

Applicants argue that Wilks et al. fail to make up the deficiencies of the primary reference. The Examiner disagrees. The rejection presented in Paper No. 7, section 7 clearly describes how Wilks et al. makes up for the deficiencies of the primary reference. Applicants have pointed to no particular deficiency for the Examiner to rebut.

Applicants argue that Wilks et al. merely suggest the desire to produce enzymes with new substrate specificities and does not suggest the "very specific process for doing so". The Examiner disagrees. Applicants themselves have argued a broad scope for which the instant methods should have protection. Furthermore, Greener et al. clearly define all the elements of the "very specific process" claimed, and Wilks et al. clearly provide the motivation to produce new stereoselectively specific enzyme activities in microorganisms other than the gram negative *E. coli*. The Examiner notes that the enantiomeric specificity of Wilks et al. is a specific form of a stereoselectivity.



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### NEW OBJECTIONS/REJECTIONS

The following new grounds are necessitated by Applicants' amendment to the pending claims and, thus, does not prohibit the **FINALITY** of the instant action.

14. Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants are required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 10 does not further limit the subject matter of its parent claim, claim 1, because the terms regio-, chemo-, and stereoselective encompass all enzymatic activity thus not materially limiting the subject matter of the parent claim.

The Examiner notes that this rejection is identical to the previous rejection of Claim 9 since canceled claim 9 and new claim 10 are drawn to the same subject matter.

15. Claims 4, 10, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greener et al. in view of Wilks et al. The Examiner notes that new Claim 10 is drawn to the same subject matter as canceled Claim 9. The original presentation of this rejection is found in Paper No. 7, section 7. Applicants traverse this rejection in Paper No. 11. The Examiner maintains this rejection in Paper No. 12, sections 6 and 13. Applicants traverse this rejection again in Paper No.

13. See above Response to Arguments.

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***Summary of Pending Objections/Rejections***

16. The following is a summary of the pending Objections/Rejections against the instant claims:
- a. Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a parent claim (New).
  - b. Claims 1-2 and 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Greener et al. (Maintained).
  - c. Claims 4 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greener et al. in view of Wilks et al. (New, but analogous to previous rejection).

***Conclusion***

17. No claims are allowed in the instant application for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

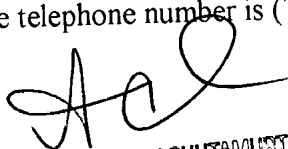
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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Kathleen M. Kerr whose telephone number is (703) 305-1229. The Examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
PONNATHAPU ACHUTAMURTHY  
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KMK

December 5, 2000